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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,530	LEGRAIN ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-16,18 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *1,3-5,7,8,12,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 6, 9-11, 16, 18 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 18 April 2005 in response to the Non-Final Office Action mailed 13 July 2004. Claims 1, 3-5, 7, 8, 12, 14 and 15 had been withdrawn from consideration and claims 2, 6, 9-11, 13 and 16-20 were considered in the 13 July Office Action. Claims 13, 17 and 19 were canceled, claims 6, 9, 11, 16, 18 and 20 were amended and claims 21 and 22 were added in the 18 April Paper. Claims 1-12, 14-16, 18 and 20-22 are pending and claims 2, 6, 9-11, 16, 18 and 20-22 are under consideration.

Response to Amendment and Arguments

Rejection of claims 13, 17 and 19 is rendered moot by the cancellation thereof.

Claim Rejections - 35 USC § 112

Rejection of claims 16 and 20 under 35 U.S.C. 112, first paragraph, as containing new matter is **withdrawn** in view of the amendments to the claims.

Rejection of claim 20 under 35 U.S.C. 112, second paragraph, as being indefinite is **withdrawn** in view of the amendments to the claims.

Claim 10 **stands** rejected and claim 21 is **newly rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record and herein below.

Claim 10 was rejected on the grounds that the specification fails to disclose the relevant identifying characteristics of the genus of variants claimed such that the skilled artisan would recognize that applicant was in possession of the claimed invention. Newly added claim 21 is directed to nucleic acid variants encoding a polypeptide having the activity of binding to βTrCP or RasSF1 and wherein the polynucleotide variant exhibits at least 95% homology with SEQ ID NO: 1 or 99.99% sequence homology with SEQ ID NO: 3. For the reasons set forth in the previous Office Actions and herein below, the application fails to adequately describe the claimed genus because the specification fails to disclose the relevant identifying characteristics of the genus.

Response to arguments

In response to the *prima facie* case and arguments of record, Applicant has amended claim 10 such that the variants are limited to having one type of modification selected from nucleotide change that is silent or produces a conservative or nonconservative amino acid substitution, and a nucleotide deletion. In the Remarks, Applicant contends that the skilled artisan would be able to distinguish the claimed variants of SEQ ID NO: 1 or 3 from variants that do not have the activity recited in the claims using the assay for the recited activity disclosed in the application.

This argument has been fully considered but is not deemed persuasive. As discussed in the previous Office Action (page 4), the amendment and remarks do not address the statements regarding descriptive support for naturally occurring allelic variants set forth in the paragraph bridging pages 4-5 of the 22 October 2003 Office Action. With regard to a description of a method for obtaining the claimed invention, as stated in the paragraph bridging pages 4-5 of the

previous Office Action, an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property (*i.e.*, it encodes a polypeptide that binds βTrCP or RasSF1) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Applicant is reminded that *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant further contends that the recitation of structural characteristics along with the recitation of function of binding either βTrCP or RasSF1 renders the claims compliant with 35 USC §112, first paragraph, written description.

This argument is not deemed persuasive because the teachings of the specification provide no structural basis for the functional properties recited in the claim. *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) states, "[w]e hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated." (at

1021). Applicant is reminded that description of a claimed genus requires not only a recitation of structural and functional characteristics but also a known or disclosed correlation between function and structure (see MPEP §2163(3)(a)(ii)). As the specification fails to describe a correlation between the structural and functional characteristics recited in the claims, the skilled artisan would not have viewed the specification as disclosing the relevant identifying characteristics of what is now claimed.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole; therefore, claim 10 stands rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description.

Claim 20 **stands rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record and herein below.

In the previous Office Actions, it was established that although the specification does not explicitly state that the claimed pharmaceutical composition is to be used for gene therapy, the only utility asserted in the specification for a pharmaceutical composition comprising a vector as set forth in claim 20 is gene therapy. The rejection set forth in the 22 October 2003 Office Action concludes that due to the art recognized unpredictability of gene therapy and the lack of guidance in the specification or prior art with regard to how to use the claimed pharmaceutical composition, it would require undue experimentation to practice the invention.

Response to arguments

In response to the *prima facie* case and arguments of record, Applicant has amended the claim to recite that the pharmaceutical composition is for use in gene therapy and contends that the claim is enabled by the specification at paragraphs 155-163 and 169 and the prior art referenced therein.

This argument has been fully considered but is not deemed persuasive. As discussed in the 22 October Office Action, the teachings in the specification provide that β-TrCP interacts with RASSF1 as evidenced by yeast two-hybrid analysis (see especially Example 6, beginning on page 37) and coimmunoprecipitation (see especially Example 8, beginning on page 40). The specification also provides that inhibition of RasSF1 expression by RNAi results in decreased β-catenin expression, while overexpression of RasSF1C results in an increase in β-catenin expression (see especially Example 12, beginning on page 47). The specification concludes, "[the] interaction of RasSF1 with βTrCP could influence the activity of RasSF1 and its tumor suppressive functions in lung, breast and ovarian tumors. In particular the precise mapping of the interaction domains on both proteins could be used to modulate the function of RasSF1 in tumorigenesis in breast, lung, and ovarian tumors in which inactivation of RasSF1 has been associated with the cancer process" (page 48). However, none of these teachings suggest a condition that might be amenable to treatment using a pharmaceutical composition comprising a recombinant host cell comprising vectors comprising the nucleic acids set forth as SEQ ID NO: 1 or 3. The teachings in the art and specification suggest that the cell of the pharmaceutical composition might have a less malignant phenotype than an unmodified cancer cell; however, the skilled artisan would have no idea how to apply such a cell as a pharmaceutical.

With regard to overcoming the problems generally faced in translation of *in vitro* findings into a successful gene therapy protocol, the specification provides only a general overview of potential gene therapy vectors known in the art. There are no teachings in the specification directed to solving the problems encountered in developing gene therapies and nothing to suggest that, even if a suitable condition for treatment had been identified in the specification, the instant claimed pharmaceutical composition could be used successfully in light of the high degree of unpredictability in the gene therapy art.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, claim 20 stands rejected under 35 USC §112, first paragraph.

Claims 2, 6, 9-11, 16, 18 and 20 **stand rejected** and claims 21 and 22 are **newly rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record and herein below.

As stated in the previous Office Action, although the relative level of skill in the art is high, the skilled artisan would not know how to use the claimed invention without first engaging in undue experimentation. The specification discloses that RasSF1 interacts with βTrCP and, based on teachings in the art showing that RasSF1A is a tumor suppressor that is inactive in some lung, breast and ovarian tumors, teaches that the skilled artisan can use nucleic acids encoding RasSF1 and βTrCP to identify agents that modulates the complex, which agents can be used to treat breast, lung, and ovarian tumors. However, there is no evidence of record to indicate that the complex of RasSF1 and βTrCP is in any way linked to any type of cancer, let alone a

target for therapeutic intervention. Thus, one of ordinary skill in the art seeking to use the claimed invention as asserted in the specification would have to establish by empirical experimentation which, if any, cancers could be treated using agents identified as modulating the RasSF1/βTrCP interaction. Given the diversity of cancers and the absence of evidence to indicate the RasSF1/βTrCP complex is a determinant in any cancer, using the invention according to the teachings of the specification would clearly require undue experimentation.

Response to arguments

In response to the *prima facie* case of record, Applicant points out that the claims presently under consideration are not directed to a screening assay for agents that modulate the complex of RasSF1 and βTrCP or to compounds identified in such an assay. Applicant contends that the issues raised in the Office Action are irrelevant to enablement for the present claims because a patent application is required only to enable an invention with respect to the claimed subject matter. In support of this position, Applicant cites *In re Moore and Janoski*, 169 USPQ 236 (CCPA 1971) and *In re Geerdes*, 180 USPQ 789 (CCPA 1974).

These arguments have been fully considered but are not deemed persuasive. With regard to the case law cited, it would seem that the Court's position in the passages cited from *In re Moore* and *In re Geerdes* is that the application need not enable embodiments that are not within the scope of the claim. In the instant case, there does not appear to be any disagreement regarding what is within the scope of the claims. As stated on page 12 of the previous Office Action, the claims are directed to nucleic acids, and compositions comprising nucleic acids encoding β-TrCP protein and RasSF1, which are demonstrated by *in vitro* assays to interact with

one another. In *In re Moore* the Court states, "[w]hat is of maximum concern in any analysis of whether a particular claim is supported by the disclosure in an application is whether that disclosure contains sufficient teaching regarding the subject matter of the claims as to enable one skilled in the pertinent art to make *and* use the claimed invention" (page 239; emphasis in original). Thus, the Court clearly indicates that the enabling disclosure must teach the skilled artisan how to use what is claimed.

As stated in the previous Office Action (page 12), "[w]ith regard to using the claimed invention, the specification teaches that the nucleic acids can be used in assays to screen for agents that modulate the interaction, which, in turn, can be used as a pharmaceutical for preventing or treating tumors (see especially paragraphs [0017], [0024], [0131], [0139], [0155]), as well as the direct administration of the nucleic acids and compositions as gene therapy". As these are the uses asserted for what is being claimed, it is incumbent upon the application to teach the skilled artisan how to use the claimed nucleic acids or agents identified therewith as pharmaceuticals.

With regard to the screening methods, Applicant contends that the methods are clearly enabled because assays such as two-hybrid screening are well known in the art and sufficient data are given in the specification to establish that protein-protein interactions between βTrCP and RasSF1 do occur. Applicant points out that the application discloses for the first time the specific interaction between βTrCP and RasSF1; underlines the importance of RasSF1 in tumorigenesis in breast, lung and ovarian cancers; and show that the modulation of RasSF1 expression has consequences on the level of other proteins such as β-catenin indicating that expression of RasSF1 and βTrCP are interconnected. Based on this, Applicant urges that the

interaction of βTrCP with RasSF1 may influence activity of RasSF1 cannot be said to be a simple speculation.

Applicant contends that the invention allows the precise mapping of the interaction domains of both proteins and defines a new approach to modulate the activity of RasSF1, by identifying a new partner that interacts with RasSF1 and can protect it form inactivation. Applicant concludes that modulators identified by the methods may prove useful in cancer therapy.

These arguments have been fully considered but are not deemed persuasive. Applicant is reminded that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson,* 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

As discussed on page 13 of the previous Office action, it has been recognized in the art for many years that "cancer" is a constellation of diseases having disparate molecular etiologies, wherein therapeutics effective in treating one type of cancer are not effective in treating many other types of cancer. Thus, the therapeutic application of an agent to the treatment of cancer requires the identification of cancers that respond to the agent. And on page 14, the Office Action points out that Damman *et al.* identify RasSF1A as a tumor suppressor and present data indicating that RasSF1A is not present in breast, lung and ovarian tumors (see especially Figure 3 and the first full paragraph on page 318 of Dammann *et al.*). Given that it is the absence of RasSF1A that the art recognizes as linked to tumorigenesis in some breast, lung and ovarian

tumors, the skilled artisan would not expect a compound that modulates a complex of RasSF1A and βTrCP, which would also be absent, to affect the cancer phenotype in these cells.

Given the unpredictability of the relevant art it is not sufficient to disclose that two proteins interact and assert that modulators identified in assays of that interaction might be useful in the treatment of cancer. There is no evidence of record to indicate that the complex of RasSF1 and βTrCP is in any way linked to any type of cancer, let alone a target for therapeutic intervention. Thus, one of ordinary skill in the art seeking to use the claimed invention as asserted in the specification would have to establish by empirical experimentation which, if any, cancers could be treated using agents identified as modulating the RasSF1/βTrCP interaction. Given the diversity of cancers, the unpredictability of the art and the early stage of development of the invention, using the claimed invention as contemplated would require undue experimentation.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §112, first paragraph.

Claim Rejections - 35 USC § 102

Rejection of claim 9 under 35 U.S.C. 102(b) as being anticipated by Cenciarelli *et al.* (1999) *Curr. Biol.* 9:1177-1179 is **withdrawn** in view of the amendments to the claim.

Rejection of claim 9 under 35 U.S.C. 102(b) as being anticipated by *Entrez* Nucleotide sequence, Accession No. AF061836 (gi:3126875) is **withdrawn** in view of the amendments to the claim.

Claims 6, 10, 11, and 20 **stand rejected** and claims 16, 21 and 22 are **newly rejected** under 35 U.S.C. 102(b) as being anticipated by Cenciarelli *et al.* (1999) *Curr. Biol.* 9:1177-1179 for reasons of record and herein below.

As described in the previous Office Action, Cenciarelli *et al.* teaches a polynucleotide comprising the sequence set forth as SEQ ID NO: 1, and a vector and host cell comprising said polynucleotide, which anticipate the limitations of claims 6, 10, 11 and 13. Furthermore, the skilled artisan would understand that the vector of Cenciarelli *et al.* would be comprised in a buffer that meets the limitations of "pharmaceutically acceptable carrier" as they are understood based on the discussion at paragraph [0130]. Thus, the teachings of Cenciarelli *et al.* also anticipate the composition of claim 20.

In response to the *prima facie* case and arguments of record, Applicant has amended claim 6 such that it is directed to a vector comprising a polynucleotide consisting of SEQ ID NO: 1, amended claim 10 such that it recites that the variant has a modification selected from a nucleotide change or a nucleotide deletion, amended claim 16 such that it is directed to a vector comprising a polynucleotide consisting of SEQ ID NO: 1, and amended claim 20 such that it is directed to a pharmaceutical composition comprising a vector comprising a polynucleotide consisting of SEQ ID NO: 1.

Claim 21 is directed to a variant of a polynucleotide designated as SEQ ID NO: 1 or 3, wherein the variant binds to βTrCP or RasSF1 and has at least 95% homology with SEQ ID NO: 1 and claim 22 is directed to a composition comprising a vector comprising a polynucleotide consisting of SEQ ID NO: 1.

In the remarks, Applicant contends that Cenciarelli *et al.* does not teach a vector comprising a polynucleotide consisting of SEQ ID NO: 1 according to claims 6, 11, 16, 20 and 22 or a variant of SEQ ID NO: 1 having the structural features as recited in claim 10. Applicant further contends that Cenciarelli *et al.* does not teach a variant having at least 95% homology with SEQ ID NO: 1 according to claim 21.

These arguments have been fully considered but are not deemed persuasive because they are based on an overly narrow reading of the claims. Claims 6, 11, 16, 20 and 22 are now directed to a vector comprising a polynucleotide consisting of SEQ ID NO: 1. Office personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). According to the broadest reasonable interpretation of the claim, a vector comprising a sequence consisting of SEQ ID NO: 1 is open to comprising any sequence in addition to SEQ ID NO: 1 because the sequence comprised by the vector is open. In other words, the claim does not exclude the vector construct of Cenciarelli *et al.* because the vector can comprise any sequence in addition to the sequence consisting of SEQ ID NO: 1.

Claim 10 is directed to "[a] variant of a polynucleotide designated as SEQ ID NO: 1" and claim 21 is directed to "[a] variant polynucleotide designated as SEQ ID NO: 1". There is

nothing in the claim language used that would exclude nucleic acids comprising the variants as claimed.

With regard to claim 10, the nucleic acid of Cenciarelli *et al.* encodes a variant of SEQ ID NO: 3 (*i.e.*, SEQ ID NO: 1, which is a variant of SEQ ID NO: 3 encoding a polypeptide having multiple nonconservative amino acid substitutions and deletions), wherein the variant binds to βTrCP. Thus, the nucleic acid comprising SEQ ID NO: 1 of Cenciarelli *et al.* anticipates the variant of SEQ ID NO: 3 according to the instant claim 10.

Likewise, with regard to claim 21, according to the broadest reasonable interpretation of the claim, the variant can comprise any variant of SEQ ID NO: 3 (*i.e.*, unlimited additions, deletions or substitutions) that has at least 95% identity to SEQ ID NO: 1. The nucleic acid of Cenciarelli *et al.* comprises a sequence that is 100% identical to SEQ ID NO: 1 and, as such, comprises a variant of SEQ ID NO: 3 that has at least 95% homology with SEQ ID NO: 1 and which binds to βTrCP. Therefore, the variant of Cenciarelli *et al.* anticipates the variant of the instant claim 21.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims are properly rejected under 35 USC §102(b) as anticipated by Cenciarelli *et al.*

Claim 10 **stands rejected** and claim 21 is **newly rejected** under 35 U.S.C. 102(b) as being anticipated by *Entrez* Nucleotide sequence, Accession No. AF061836 (gi:3126875), published 9 May 1998 (hereinafter, AF061836) for reasons of record and herein below.

The previous Office Action states, "AF061836 discloses a nucleic acid comprising a sequence that is 98.2% identical to the instant SEQ ID NO: 3 over its full length. Thus, AF061836 anticipates the variant of claim 10" (page 13).

In the remarks, Applicant contends that AF061836 does not anticipate amended claim 10 because the claimed variant is limited to presenting with *one* type of modification, *i.e.*, either a nucleotide modification or nucleotide deletion, but not both types of modifications. This argument is not deemed persuasive because the claim actually recites, "said variant having one type of modification". According to the broadest reasonable interpretation of the claim, the variant is limited only to comprising one type of modification (*i.e.*, at least one) and can comprise other modifications in addition to the one that is required. It is further noted that there appears to be no support in the originally filed application for a variant limited to comprising only one type of modification and no other type of modification. Therefore, any claim to a variant limited to having a modification consisting of a nucleotide change or a nucleotide deletion would constitute impermissible new matter.

Applicant contends that the nucleic acid set forth in AF061836 does not anticipate claim 21 because the claim is directed to a variant having at least 99.99% homology with SEQ ID NO: 3. This argument is not persuasive because claim 21 recites "[a] variant of polynucleotide designated as... SEQ ID NO: 3". There is no definite article preceding polynucleotide to indicting that the claimed polynucleotide variant is limited to having 99.99% homology with the entire sequence set forth as SEQ ID NO: 3. Thus, the claim encompasses any variant having 99.99% homology with any portion of SEQ ID NO: 3. The sequence from nucleotide 84 to nucleotide 1084 of AF061836 is identical to the instant SEQ ID NO: 3 from nucleotide 1 to

nucleotide 1620 except for a single mismatched nucleotide at nucleotide 1122 of SEQ ID NO: 3. This portion of the AF061836 sequence is therefore >99.99% identical to a polynucleotide designated as SEQ ID NO: 3.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims are properly rejected under 35 USC §102(b) as anticipated by AF061836.

New Grounds Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The MPEP states, "[i]f new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. §112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." (MPEP § 2163.06). The MPEP further states, "[w]henever the issue arises, the fundamental factual inquire is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was

filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in the application" (*Id.*, § 2163.02). The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996).

The instant claim 21 is directed to a variant having at least 99.99% homology with SEQ ID NO: 3. In the remarks, page 5, Applicant asserts that support for the limitations can be found in the last paragraph on page 10. It is assumed that Applicant is referring to paragraph 0074, which is actually the second paragraph on page 11. The paragraph states, "variants can also have 96%, 97%, 98%, and 99.999% sequence identity to the reference polynucleotide". There is no support for a polynucleotide having 99.99% homology with a reference sequence in the originally filed disclosure. Therefore, the limitation constitutes impermissible new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is indefinite in being directed to "[a] variant of polynucleotide designated as..." It is unclear whether the claim is encompasses a variant of a polynucleotide designated as SEQ ID NOs:1 or 3 having the recited homology or is limited to a variant of the polynucleotide polynucleotide designated as SEQ ID NOs:1 or 3 having the recited homology. As such, the metes and bounds of the claimed invention are unclear.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636